

WHAT IS CLAIMED AS NEW AND DESIRED TO BE SECURED BY LETTERS
PATENT OF THE UNITED STATES IS:

1. A method for controlling the lineage development in an *in vitro* human tissue system, comprising culturing human stem and/or progenitor cells in a liquid culture medium which is replaced at a rate of about 1 ml of medium per 1 ml of culture per about 24 to about 48 hours, and removing metabolic products and replenishing depleted nutrients, while maintaining said culture under physiologically acceptable conditions, and adjusting the concentration of hematopoietic growth factors to select for enhanced production of a desired cell type.

2. The method of Claim 1, wherein at least one member selected from the group consisting of human peripheral blood mononuclear cells, human bone marrow cells, human fetal liver cells, human cord blood cells, human spleen cells and mixtures thereof are cultured.

3. The method of Claim 1, wherein said cells comprise human stromal stem and/or progenitor cells and/or mature stromal cells.

4. The method of Claim 1, wherein said cells comprise human bone marrow stromal cells.

5. The method of Claim 1, wherein B-cells and T-cells are depleted and said medium is substantially free of IL-2.

6. The method of Claim 1, wherein active and prolonged erythropoiesis is achieved by adding IL-3 and Epo to said medium.

7. The method of Claim 6, wherein GM-CSF is added to said medium.

8. The method of Claim 1, wherein active and prolonged granulopoiesis is achieved by adding IL-3 and GM-CSF to said medium.

9. The method of Claim 1, wherein malignant cells are depleted.

10. The method of Claim 1, wherein said human cells comprise genetically transformed stem and/or progenitor cells.

11. The method of Claim 1, wherein said medium is replaced continuously.

12. The method of Claim 11, wherein replacement of said medium comprises perfusing fresh medium through at least part of the mass of said human stem cells.

13. The method of Claim 1, wherein said medium is replaced periodically or intermittently.

14. The method of Claim 13, wherein replacement of said medium comprises perfusing fresh medium through at least part of the mass of said human cells.

15. The method of Claim 1, wherein said medium comprises animal or human sera or plasma.

16. The method of Claim 1, wherein said medium is substantially serum free.

17. The method of Claim 1, wherein said media comprises a corticosteroid.

18. The method of Claim 1, comprising maintaining glucose concentration in said medium in the range of from 5 to 20 mM, lactate concentration in said medium below about 35 mM, glutamine concentration in said medium in the range of from 1 to 3 mM, and ammonia concentration in said medium below 2.4 mM.

19. The method of Claim 1, further comprising removing nonadherent cells continuously, periodically, or intermittently, without disturbing adherent cells.

20. A method for assaying the effect of a substance or physical condition on a human hematopoietic cell mass, comprising culturing a first portion of said human hematopoietic cell mass, including dividing human stem cells and progenitor cells, in a liquid culture medium which is replaced, either continuously, periodically, or intermittently, at a rate of about 1 ml of medium per ml of culture per about 24 to about 48 hour period in the presence of said substance, and removing metabolic products and replenishing depleted nutrients while maintaining said culture under physiologically acceptable conditions, and comparing the compositional profile of the human hematopoietic cell mass to the profile of a second portion of said human hematopoietic cell mass cultured identically but in the absence of said substance or physical condition.

21. The method of Claim 20, wherein said substance is selected from the group consisting of hematopoietic growth factors, synthetic agents, hormones and toxins.

22. The method of Claim 20, wherein said substance is a monoclonal antibody specific for a compound endogenously produced by said hematopoietic cell mass.

23. The method of Claim 20, wherein said substance is an antagonist of a compound endogenously produced by said hematopoietic cell mass.

24. The method of Claim 20, wherein said physical condition is selected from the group consisting of pressure, temperature, exposure to light, gravity, and combinations thereof.

25. A functioning *in vitro* human tissue system, comprising (i) a chamber containing human hematopoietic cells, including dividing human hematopoietic stem cells and progenitor cells cultured in a liquid culture medium, wherein said chamber contains a surface for the attachment of adherent cells (ii) means for replacing, either continuously or periodically, said liquid culture medium at a rate of about 1 ml of medium per ml of culture per about 24 to about 48 hour period, (iii) means for exposing said liquid culture medium to an oxygen-containing gas, and (iv) means for removing metabolic products and replenishing depleted nutrients while maintaining said culture under physiologically acceptable

conditions to thereby maintain a functioning, reconstructed in vitro bone marrow tissue.

26. The system of Claim 25, wherein said chamber comprises two compartments separated by a membrane which is permeable to oxygen and carbon dioxide, allows for cell or extracellular matrix attachment, and is impermeable to water, wherein one of said compartments contains said liquid culture medium and the other of said compartments contains said oxygen-containing gas.

27. The system of Claim 25, further comprising (v) means for removing nonadherent cells continuously, periodically, or intermittently, without disturbing adherent cells.

28. The system of Claim 25, further comprising (vi) means for removing at least a portion of adherent cells in a viable and functional state.

29. The system of Claim 25, further comprising (v) means for removing nonadherent cells continuously, periodically, or intermittently, without disturbing adherent cells and (vi) means for removing at least a portion of adherent cells in a viable and functional state.

30. The system of claim 25, wherein said human hematopoietic cells are selected from the group consisting of human peripheral blood mononuclear cells, human bone marrow cells, human fetal liver cells, human cord blood cells, human spleen cells, and mixtures thereof.

31. The system of Claim 25, wherein said human hematopoietic cells comprise human stromal stem and/or progenitor cells and/or mature stromal cells.

32. In a method of bone marrow transplantation, comprising obtaining a tissue sample from a donor, culturing said tissue sample, and implanting said tissue sample in a donee, wherein the improvement is said culturing comprises culturing said tissue, which comprises a mass of human stem cells, in a liquid culture medium which is replaced, either continuously or periodically, at a rate of about 1 ml of medium per ml of culture per about 24 to about 48 hour period, and removing metabolic products and replenishing depleted nutrients while maintaining said culture under physiologically acceptable conditions.

33. The method of Claim 32, wherein said tissue sample implanted in said donee comprises genetically transformed stem and/or progenitor cells.

34. The method of Claim 32, wherein said donee is said donor.

35. The method of Claim 32, wherein said donee is not said donor.